

# Reply to: "AST/platelet ratio index associates with progression to hepatic failure and correlates with histological fibrosis stage in Japanese patients with primary biliary cirrhosis"

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# Accepted Manuscript

Letter to the Editor

Reply to: “AST/platelet ratio index associates with progression to hepatic failure and correlates with histological fibrosis stage in Japanese patients with primary biliary cirrhosis”

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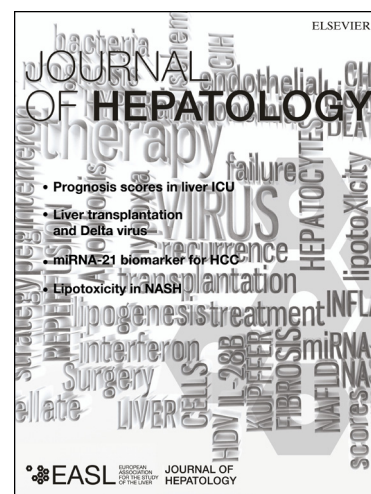
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**Reply to: “AST/platelet ratio index associates with progression to hepatic failure and correlates with histological fibrosis stage in Japanese patients with primary biliary cirrhosis”**

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ACCEPTED MANUSCRIPT

*To the Editor:*

We read with interest Joshita and colleagues' letter regarding our original article [1]. In taking the time to present their important Japanese data [2], the authors provide further independent validation of AST/platelet ratio (APRI) in risk stratification of patients with primary biliary cirrhosis (PBC). As the authors surmise, whilst the demography of our cohorts was varied it was not representative of all populations globally, and the robustness of any observation – even if simple and low cost as in this case – is in validation more so than discovery.

PBC is not a benign, homogeneous autoimmune liver disease; and although present disease nomenclature needs improvement, the current sole therapy - ursodeoxycholic acid (UDCA) - still leaves a substantial cohort of individuals at risk from life-threatening progressive disease and impaired quality of life. Risk stratification is therefore of value to identify individuals with PBC who will benefit from new treatment and as illustrated herein, APRI at baseline or reapplied 1-year following therapy (APRI-r1) represents an additive tool in identifying those patients at risk of adverse clinical outcome with high accuracy. Joshita et al. also report good correlation between APRI and disease stage; [2] however, it is apparent in both studies that a significant proportion of patients have an APRI >0.54 despite histological evidence of early stage (I-II) disease. Moreover, in our study we were able to show that in those without objective evidence of cirrhosis APRI retains independent predictive value thus supporting APRI/APRI-r1 as a prognostic, clinically meaningful utility beyond application as a surrogate for liver fibrosis.

The ability to reliably predict outcome in patients with PBC is beneficial for patient counselling, timing of diagnostic procedures and therapeutic intervention. In this regard, prospective evaluation of APRI-r1 in terms of additive value to existing UDCA response criteria is of clear importance; particularly given the potential use of surrogate endpoints in development of new treatments in PBC [3–5]. Our observations alongside those of Joshita et al., further substantiate the role stratification could play not just in clinical practice but also in clinical trial design. Hence future therapeutic trials in PBC should consciously consider inclusion criteria beyond classic response criteria, and such stratifiers may include additional tools such as liver elastography and APRI-r1. Finally as is evident by our studies, in the pursuit of optimal management for a rare disease such as PBC, methodologically robust, internationally representative, numerically well-powered cohorts are essential in order to allow investigators to make clear replicated observations about disease nature, course and intervention.

**Conflicts of interest**

None

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